

units spread over 10 days. The chancre healed up and the Wassermann and Kahn reactions both became negative after rather more than 5 weeks and have remained negative for several months. This agrees with the results published in the United States of America in a small series of cases and there are now many cases in which the results are apparently excellent, but no final conclusions can be drawn until sufficient time has elapsed to show that there are no recurrences. It looks as if penicillin were going to prove effective with both the chief venereal diseases; it may take the place not only of the sulphonamides for gonorrhoea but of the arsenicals for syphilis.

PENICILLIN IN VENEREAL DISEASES—2*

By JACK SUCHET, M.R.C.S., L.R.C.P.

Assistant Director, Venereal Diseases Department, and Senior Assistant, Department of Obstetrics and Gynaecology, St. Mary's Hospital, London

The use of penicillin, of which Sir Alexander Fleming is the discoverer, in the treatment of venereal diseases has not been systematic. We have used it, rather, during a research programme; we have, however, treated all sorts of venereal diseases from the chancroidal type of lesion on the vulva in the female to acute gonorrhoea in the male. We have treated one case of primary syphilis and one of tabes dorsalis. We have also tried penicillin in non-specific urethritis. We have thus gone through the whole range of venereal conditions. Our cases are much too small in total number to provide any definite conclusions and the results are clinical "impressions" only. Altogether we have treated 70 cases in the venereal diseases department.

Gonorrhoea

Taking first acute gonorrhoea in males, our treatments have varied from single injections at 10-minute intervals to multiple injections at intervals of a varying number of hours. We have also used the continuous drip. No matter what the dosage has been, our results have been surprisingly good. Nevertheless in some cases there have been relapses which we did not anticipate. Of the patients who were treated by the single injection method, there was only one failure among 7 cases. In these patients the discharge cleared up completely within 24 hours, the gonococci having disappeared within 12 hours. In the one case, however, the patient relapsed 2 days later but finally responded to treatment with a different dosage.

The suitable amount to be used for the treatment of gonorrhoea appears to be between 100,000 and 120,000 units. What seems to be important is the time factor. In those people to whom we have given 120,000 units over a long interval—giving them perhaps 15,000 unit doses at 3-hourly intervals for 8 doses—our results have been better than they would have been if the whole total dose had been given straight off. Both the calcium and the sodium salts were used. At first we were wary of using the former, but some patients were given 100,000 units in a single injection and there was very little local reaction after the intramuscular injection. Some patients did have a little pain, ranging from a local numbness to a cramp, but it did not last long nor did it upset the patient even when a large dosage of 100,000 units was used. There was no ill effect—no general toxic effect—no matter what dosage of penicillin was employed. When it was given intravenously the only noticeable effect was that the patient complained of a burning sensation at the site of the infection. In the case of a gonococcal arthritis, for example, there was a sense of warmth in the joint.

In one case an application in ointment form into the urethra was tried but the result was not a success. This man, however, was eventually cured without further treatment, although he was sulphonamide-resistant.

* An address to the Medical Society for the Study of Venereal Diseases, 20th May 1944.

PENICILLIN IN VENEREAL DISEASES

As a rule, no matter what the original dosage, the gonococci disappeared within 4 hours, in some cases within $1\frac{1}{2}$ hours. The next thing one noticed was that a few hours later the discharge increased in amount and became mucoid in character. A smear of this profuse discharge revealed masses of leucocytes but no gonococci. Gradually the discharge cleared up. Some people have reacted very oddly to the treatment: the discharge continued as long as 8 days, and if they had been treated with sulphonamide it would have been said that they were certain to relapse, but there was a final cure. In one female case, after treatment the gonococci disappeared; they then recurred in the urethra and cervix, yet without further treatment they disappeared again. Although there have been failures none of them were complete; they always responded to further treatment with penicillin. We can, I think, always get a cure; it is only a question of using sufficient penicillin.

Are penicillin-fast cases going to occur? Organisms can be made fast to penicillin, but since the gonococcus is the most susceptible to penicillin, this does not seem likely to occur. Furthermore, the impression is gathered that a patient who has been previously treated with sulphonamide and has failed to respond, reacts better to penicillin than do untreated cases. Whatever may be the explanation, the fact remains that in this small number of patients there have been more failures in untreated cases than in cases which had had treatment.

Only 4 women were treated and all with success. The minimum dosage employed was 60,000 units in a continuous drip for $9\frac{1}{2}$ hours, and the maximum was eight 3-hourly injections of 15,000 units each, intramuscularly. While on the subject of gonorrhoea in females, I may add that one case of gonococcal pyosalpinx has just been treated and seems to have responded well.

Gonococcal arthritis.—Four cases of gonococcal arthritis have been treated also with doses varying from 700,000 units to 300,000, and a man who received the smallest amount of penicillin—namely, 300,000 units in 3 days—did best of all. This man had been crippled for $3\frac{1}{2}$ years and had had the usual treatments. Within 24 hours after the administration of penicillin had been begun all the pain disappeared and he was left with little more than some residual stiffness of his joints. He was given massage and movements and is now back at his work as a lorry driver. In another case of gonococcal arthritis, however, there was improvement while the patient was receiving penicillin, but this was always followed by a relapse. A third patient was suffering from what might have been a gonococcal arthritis—the history was suggestive, although we never found the gonococcus. He was acutely ill and numerous joints, both small and large, were affected. There was bilateral iridocyclitis and both feet were covered with keratodermic blennorrhagic vesicles. The patient was given penicillin treatment and within 3 days his arthritis cleared up and he was perfectly well for about a month. At the end of that time there was a relapse in a few joints, but the patient was given a further course of treatment and then recovered. It might be mentioned that the keratodermic vesicles dried up and scaled off within one week of the commencement of treatment.

Differential diagnosis.—Sir Alexander Fleming has described the way in which, by means of penicillin, it is possible to differentiate various organisms. This has been our own experience. In one case—a child with non-specific vulvovaginitis—there were a number of relapses. In this case, by using penicillin to cover part of the culture plate, we were able to prove the presence of penicillin-resistant organisms, so that the relapses were in accordance with our expectations.

Dosage.—There has never been a failure after the use of a large dosage of 120,000 units spread over 24 hours, although when the same dosage was given in a single injection or in 4 one-hourly injections failures have occurred. The optimum type of treatment has not been established but the dosage has been defined. It may be that a constant low level of penicillin will give a better result than a fluctuating amount of penicillin in the body.

Syphilis

Primary syphilis.—A man with primary syphilis whom we treated received

1,200,000 units over a course of 10 days. On dark-ground examination the spirochaetes were found to have disappeared from the sore within 12 hours. The initial cleansing of the chancre was likewise dramatic; it became a sterile ulcer at the end of 12 hours. Healing was very slow indeed and the chancre did not finally disappear until about 3 weeks later. It is now 5½ months since that case was treated. The Wassermann was negative 32 days after the completion of treatment, the Kahn was negative a few days later and the cerebrospinal fluid was normal both before and after treatment.

Neurosyphilis.—The other case of syphilis which was treated was one of advanced tabes dorsalis and the patient had a perforating ulcer of the foot. He was given intrathecally increasing doses of penicillin, by means of repeated lumbar punctures, during 10 consecutive days. An initial concentration of 500 units per cubic centimetre was given and when 2,000 units per cubic centimetre had been administered he could not take any more. That concentration seems to be toxic to the theca, as a few meningeal reactions developed; there was an increase in the amount of protein and of the number of cells. The perforating ulcer of the foot was connected with a small sinus which was suppurating. Penicillin was introduced into the sinus after all other treatment had failed. The penicillin treatment was successful in getting rid of the pus and the foot is now completely healed.

Interpretation of results

The question remains as to whether we have here for the first time a drug which is effective in both syphilis and gonorrhoea. If penicillin only masks the symptoms of syphilis and fails to eradicate the disease, we may be faced with a new problem. For example, a patient suffering from both gonorrhoea and syphilis, contracted at the same time, might quite conceivably not be recognized as suffering from syphilis, owing to the action of penicillin in masking the disease.

Another feature worth mentioning concerns the treatment of failures. Although patients sometimes failed to respond to a moderate dose of penicillin, when a second course of a similar dosage was given they generally got well; further, in cases of gonorrhoea, if failure was experienced after the first dose and the patients had already been found to be sulphonamide-resistant, if they were subsequently treated with sulphonamides they appeared to get well. It would not do to be too definite, but it is felt that gonorrhoea can always be cured by the use of penicillin; with regard to syphilis, however, it remains to be seen whether or not such an optimistic verdict can be pronounced.

DISCUSSION ON THE PRECEDING PAPERS

Brig. Osmond (the President), said that it had been very interesting to hear these two addresses, because it seemed as though penicillin were going to solve a great many of the problems of venereal disease. At any rate, it was encouraging to know that the gonococcus was one of the most sensitive organisms. As regards the dosage in gonorrhoea cases, from the small experience he had had, he had gathered that about 20,000 units every 2 or 3 hours up to a total of 100,000 gave the best results. Syphilis was curable and so, he was told, were granuloma inguinale and chancroid.

One of the problems which would have to be solved by the experts was to find some means of delaying the excretion of the penicillin. He had heard of a case in which penicillin was given intentionally at a time when the patient's kidneys were not working too well. In that case a comparatively small dose worked just as well as—or better than—a large dose was expected to do. It was just one case but was rather significant.

With regard to penicillin-fastness, he hoped that the medical profession would not have the same experience as they had had with the sulphonamides, and that everybody would use penicillin in adequate doses. If penicillin-fast cases were to occur, it would be the result of under-dosage. The statement that sulphonamide-resistant cases which were afterwards treated with penicillin appeared to react better than did cases treated with penicillin from the outset was interesting, because the surgeons had found that penicillin plus sulphonamide used locally in wounds was far more effective than either of the two alone.

The other point he would like to emphasize was the fact that penicillin given by intramuscular or subcutaneous injection did not get into the cerebrospinal fluid in anything like the same amount as into the blood. That might be very important in treating meningo-vascular syphilis. He had